

CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492,

497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and

5 (c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 10 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-15 404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any of the foregoing polynucleotide sequences.

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3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NOs: 122 and 198-204.

4. An isolated polynucleotide encoding at least 15 amino acid residues of a colon tumor protein, or a variant thereof that differs in one or more substitutions, 25 deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID Nos: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41,

46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 5 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-10 1081, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 2, 15 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 20 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any of the foregoing 25 sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156,

168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081.

- 10 7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081 under moderately stringent conditions.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.

10. A host cell transformed or transfected with an expression vector

according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a colon tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

5 17. A pharmaceutical composition, comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- 10 (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 15 (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

20 19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant
25 induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

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28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

5 29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

10 (a) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and

15 (c) complements of sequences of (i) or (ii) encoded by a polynucleotide recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;

and thereby inhibiting the development of a cancer in the patient.

20 30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is colon cancer.

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32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(ii) complements of the foregoing polynucleotides;
wherein the step of contacting is performed under conditions and for a time
5 sufficient to permit the removal of cells expressing the antigen from the sample.

10 34. A method for inhibiting the development of a cancer in a patient,
 comprising administering to a patient a biological sample treated according to the method
 of claim 32.

(a) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting

20 of:

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and

under conditions and for a time sufficient to permit the stimulation and/or

expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

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37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

10 38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

15 (i) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081

20 (2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

25 (iii) antigen presenting cells that expresses a polypeptide of (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

5 (i) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

10 (1) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and

15 (3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that express a polypeptide of (i);
such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

20 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

25 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the

(c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

20 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

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46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

5 47. A method according to claim 44, wherein the cancer is a colon cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

25 50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

- (a) one or more antibodies according to claim 11; and
- (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized

on a solid support.

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

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57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238,

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